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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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MARSHALL, GERSTEIN & BORUN LLP
233 S. WACKER DRIVE, SUITE 6300
SEARS TOWER
CHICAGO, IL 60606

EXAMINER	
MERTZ, PREMA MARIA	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 07/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/751,242	ISHIKAWA ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-3 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-3 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

1. Original claims 1-3 are pending in the instant application.

Specification

2. The entire amino acid sequence of G-CSF is recited in claim 1. It is suggested that the amino acid sequence be identified only by the appropriate sequence identifier as set forth in the "Sequence Listing" as required by 37 CFR § 1.821(d). Applicants are requested to delete the recitation of the sequences from claim 1 and only recite the SEQ ID NO. Furthermore, reciting the entire amino acid sequence in the claim is awkward, difficult to consider and increases the possibility of printer errors.

Claim Rejections - 35 USC § 112, first paragraph

3. Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a chemically-modified protein comprising the amino acid sequence set forth in SEQ ID NO:1 or 2, does not reasonably provide enablement for a chemically-modified protein as recited in claim 1, said protein "substantially having the amino acid sequence...". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with this claim.

With respect to claim 1, the specification does not enable a protein "substantially having...". The specification does not enable the skilled artisan to make and/or use polypeptides that have essentially the same amino acid sequence as the one disclosed. The issue here is how substantial must the sequence identity be, and what amino acids constitute this identity? The specification does not teach which residues can be conservatively substituted without affecting the functional activity of the receptor protein. It is known to the skilled artisan that conservative

amino acid substitutions outside of the active site of a protein will not affect the functional activity of the protein; however, amino acid substitutions, even conservative alterations, within the active site can inactivate the protein or change its functional activity. Absent the specific degree of sequence identity, it is unpredictable if the claimed protein would also possess the same activity as the polypeptide having the amino acid sequence of SEQ ID NO:1 or 2. Thus, without guidance as to which residues can be conservatively substituted, the skilled artisan would not be able to make and/or use polypeptides consisting essentially of the same amino acid sequence as the polypeptide having the amino acid sequence of SEQ ID NO:1 or 2.

There is no guidance provided in the specification as to how one of ordinary skill in the art would generate a G-CSF polypeptide other than the ones exemplified in the specification. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of claims, in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the

prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 112, second paragraph

4. Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because the metes and bounds of the limitation "substantially having the following amino acid sequence" is undeterminable. Either a protein has that amino acid sequence or it doesn't. If this limitation is intended to encompass a protein having other than the recited amino acid sequence, as implied by the presence of the word "substantially, it is unclear how far an amino acid sequence can deviate from the recited amino acid sequence and still be encompassed by the claims.

Claims 2-3 are rejected as vague and indefinite insofar as they depend on the above claim for their limitations.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 1 and 2 are rejected under 35 U.S.C. 102(e) as being anticipated by the Shaw patent (4,904,584). The instant claims encompass the "PEG-ylated" G-CSF described in Example 9 of the Shaw patent (column 16, lines 14-36).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Ono et al. patent (4,833,127) in view of the Davis et al. patent (4,179,337).

The Ono et al. patent disclosed an isolated and purified protein of human origin, which is identified therein as G-CSF (see abstract; column 1, lines 5-14). A comparison of the partial amino acid sequence presented at lines 50 to 54 in column 2 of Ono et al. with the amino acid sequence presented on page 4 and claim 1 of the instant application supports the conclusion that the G-CSF protein of Ono et al. is the same as the G-CSF polypeptide of the instant invention. The G-CSF protein of Ono et al. is not encompassed by the instant claims because it does not have a polyethylene glycol molecule covalently attached thereto.

As indicated by its abstract, the Davis et al. patent teaches the covalent attachment of polyethylene glycol molecules to a polypeptide to "protect the polypeptide from loss of activity".

It further teaches that such derivatized polypeptides "can be injected into the mammalian circulatory system with substantially no immunogenic response". The text at lines 44 to 51 in column 3 of Ono et al. expressly taught that peptide hormones were suitable targets for this modification.

An artisan of ordinary skill in the art of molecular biology would have found it *prima facie* obvious to have conjugated the G-CSF protein of Ono et al. to polyethylene glycol as taught by Davis et al. to protect that polypeptide from loss of activity and avoid an immunogenic response from an organism to which it was administered.

Claim rejections-Double Patenting

Statutory type (35 U.S.C. 101) double patenting rejection

7. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process .... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

7a. Claims 1-3 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-3 of copending Application No. 10/750,797. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

7b. Claims 1-3 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-3 of copending Application No. 10/436,784. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Non-statutory double patenting rejection (obviousness-type)

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8a. Claims 1-3 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2 of Patent No. 5,824,778. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the patented claims is encompassed in its entirety by the pending claims.

Claims 1-2 of U.S. Patent No. 5,824,778 (having all common inventors with the instant application), claims a G-CSF protein having at least one PEG molecule attached to at least one amino acid of the polypeptide. In instant claim 1, a G-CSF protein prepared by binding PEG to the G-CSF protein is claimed

Instant claims 1-3 are generic to claim 1 in U.S. Patent No. 5,824,778 and encompasses subject matter to which the issued claims are a species because the issued claims recite at least one PEG molecule covalently linked to the G-CSF polypeptide. However, the patented claims are obvious from the instant claims because the patented claims are directed to one specific embodiment encompassed by the instant claims. The patented product is included in instant claims 1-3. It would have been obvious to one of ordinary skill in the art at the time the present invention was made, that a G-CSF polypeptide prepared by binding PEG encompassed the species claims in the patents. The patented claims if infringed upon would also result in infringement of the broad claim of the instant application. Allowance of the pending claim, therefore, would have the effect of extending the enforceable life of the allowed claims beyond the statutory limit.

8b. Claims 1-3 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of Patent No. 6,166,183. Although the

conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the patented claims is encompassed in its entirety by the pending claims.

Claims 1-4 of U.S. Patent No. 6,166,183 (having all common inventors with the instant application), claims a G-CSF protein having at least one PEG molecule attached to at least one amino acid of the polypeptide. In instant claim 1, a G-CSF protein prepared by binding PEG to the G-CSF protein is claimed

Instant claims 1-3 are generic to claims 1-4 in U.S. Patent No. 6,166,183 and encompasses subject matter to which the issued claims are a species because the issued claims recite at least one PEG molecule covalently linked to the G-CSF polypeptide. However, the patented claims are obvious from the instant claims because the patented claims are directed to one specific embodiment encompassed by the instant claims. The patented product is included in instant claims 1-3. It would have been obvious to one of ordinary skill in the art at the time the present invention was made, that a G-CSF polypeptide prepared by binding PEG encompassed the species claims in the patents. The patented claims if infringed upon would also result in infringement of the broad claim of the instant application. Allowance of the pending claim, therefore, would have the effect of extending the enforceable life of the allowed claims beyond the statutory limit.

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (571) 272-0829.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prema Mertz

Prema Mertz Ph.D.
Primary Examiner
Art Unit 1646
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